TABLE I. Patient Characteristics

Patient	Age	Sex	Previous therapy	Before				After				Response[a] (mo)/toxicity (WHO)	Cycles (no.)
				Stage	BM	Hb (g/dl)	Lymph (10^9/L)	Stage	BM	Hb (g/dl)	Lymph (10^9/L)		
1	71	M	CLB-PDN	IV-C	D	10.1	14.9	IV-C	D	9.4	12	SD-11	4
2	76	M	CLB-PDN-EDX	IV-C	D	10.2	139	II-A	ND	11.3	55	PR-11	4
3	61	M	COP	II-B	non-D	13.2	11.9	II-B	ND	11.4	10.8	SD-14	4
4	67	M	CHOP/ CLB-IFN/RT	IV-C	non-D	9.5	12.4	IV-C	ND	7.3	28	PD (WHO-2, inf)	1
5	55	F	CLB-PDN	III-B	ND	10.8	212	II-B	ND	12.2	154	PR-7	5
6	59	M	CLB	II-B	non-D	12.9	18.3	II-B	ND	13	17	SD-1	4

ND, not done; PD, progressive disease; SD, stable disease; PR, partial remission; COP, cyclophosphamide, oncovin, prednisone; CHOP, COP plus doxorubicin.
[a]According to NCI criteria (Cheson et al. [5]).

(PD) was registered in one patient. Median time to disease progression for patients in PR or SD was 9 months (range, 1–14 months) (Table I).

The results of the present study, although based on a small number of patients, are in keeping with good compliance with this novel "fully-oral" drug regimen, including IDA given on alternate days. By contrast, the administration of IDA on alternate days, producing long-standing but lower peaks of idarubicinol (IDAol), the active metabolite, may result either in reduced toxicity or in enhanced antineoplastic activity [1].

Finally, the tendency for physicians treating patients with low-grade malignancy to prefer combination regimens suggests that oral IDA combined with alkylating agents could be worthy of exploration, particularly in elderly patients who are less disposed to receive more intensive regimens. This is especially true in CLL disease, in which dose intensity and schedule are not mandatory for delivering therapy with curative intent.

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In Vivo CAMPATH-1 Monoclonal Antibodies: A Novel Mode of Therapy for Acute Graft-Versus-Host Disease

To the Editor: CAMPATH-1 is a rat antihuman monoclonal antibody (MAb) that recognizes the CDw52 cell surface marker, an antigen expressed on the surface of nearly all normal and malignant human lymphocytes but not found on normal hematopoietic stem cells [1]. Exposing bone marrow cells (BM) to CAMPATH-1 in vitro results in substantial in vivo depletion of T cells, due to the removal of T cells bound to the IgG2b MAb by the recipients Fc receptor-positive reticuloendothelial cell system following infusion of the BM [2].

It is known that BM treatment with CAMPATH-1, which results in sufficient removal of donor T cells effectively prevents graft-versus-host disease (GVHD). Studies have demonstrated that anti-T-cell MAb can be used for the prevention and treatment of GVHD, as mature donor T cells play a dominant role in the induction of GVHD [1]. Recently, CAMPATH-1 has been administered in vivo, as part of the pre-bone marrow transplantation (BMT) conditioning, in an attempt to prevent graft rejection, for remission induction in patients with resistant lymphoid malignancies and for the treatment of severe autoimmune disorders, especially rheumatoid arthritis [3]. In addition, antithymocyte globulin and anti-interleukin-2 (IL-2) receptor antibodies have occasionally been used successfully in steroid-resistant GVHD [4].

CAMPATH-1 may therefore be of theoretical benefit in treating aGVHD. We describe a CML patient with grade IV GVHD, with major consequences to the liver who responded to CAMPATH-1 administration and 4 years post-BMT with minimal chronic GVHD. We conclude from the case presented that CAMPATH-1 administration may be of benefit in the treatment of aGVHD.

A 40-year-old woman with Philadelphia (Ph)-positive CML in first chronic phase was admitted for allogeneic BMT. The conditioning included cyclophosphamide (60 mg/kg × 2), 1,200 cGy total body irradiation (200 cGy × 6) and i.v. CAMPATH-1G (kindly provided by Dr. G Hale and Dr. H Waldmann, Cambridge, UK), 10 mg/day for 4 days pre-BMT. She received non-T-cell-depleted BM (3.38×10^8 viable cells/kg) from her HLA-matched, MLC nonreactive sister. As anti-GVHD prophylaxis, the patient received i.v. Cyclosporin A (3 mg/kg/day).

Engraftment occurred with a white blood cell (WBC) count of $>1.0 \times 10^9$/L on day +22, ANC $> 0.5 \times 10^9$/L on day +24, and untransfused platelet count $>25 \times 10^9$/L on day +30. Post-BMT, the patient had become Ph-chromosome negative. At $1\frac{1}{2}$ months post-BMT, she developed grade IV GVHD manifested by skin rash (biopsy-proven) and disturbed liver function tests (LFT). Oral Cyclosporin A (6 mg/kg/day) and p.o. prednisone 1 mg/kg/day was introduced without improvement. She was hospitalized 3 weeks later due to progression of the grade IV GVHD with liver dysfunction (ALT 348 U/L, AST 172 U/L, ALP 410 U/L, GGTP 1,123 U/L, and bilirubin 284 μmol/L). She was treated with i.v. Cyclosporin A (3 mg/kg/d) and i.v. solumedrol (5 mg/kg/day) for 3 days with no response. The patient's LFT deteriorated dramatically (ALT 434 U/L, AST 110 U/L, ALP 735 U/L, GGTP 1,190 U/L, billirubin 787 μmol/L, albumin 28 g/L).

Because of the patient's unresponsiveness to conventional treatment, I.V. CAMPATH-1G (10 mg/day) was administered for 4 days, which caused fever, chills, and response to antipyretics. Following CAMPATH-1, LFT began to return to normal, bilirubin first, followed by ALT and ALP, which gradually diminished 10–14 days later (Fig. 1). One month after initiation of CAMPATH-1, LFT showed the following results: ALT 192 U/L, AST 61 (U/L, ALP 328 U/L, GGTP 1,347 U/L, and bilirubin 36 μmol/L. On a maintenance dose of Cyclosporin A and prednisone, skin manifestations

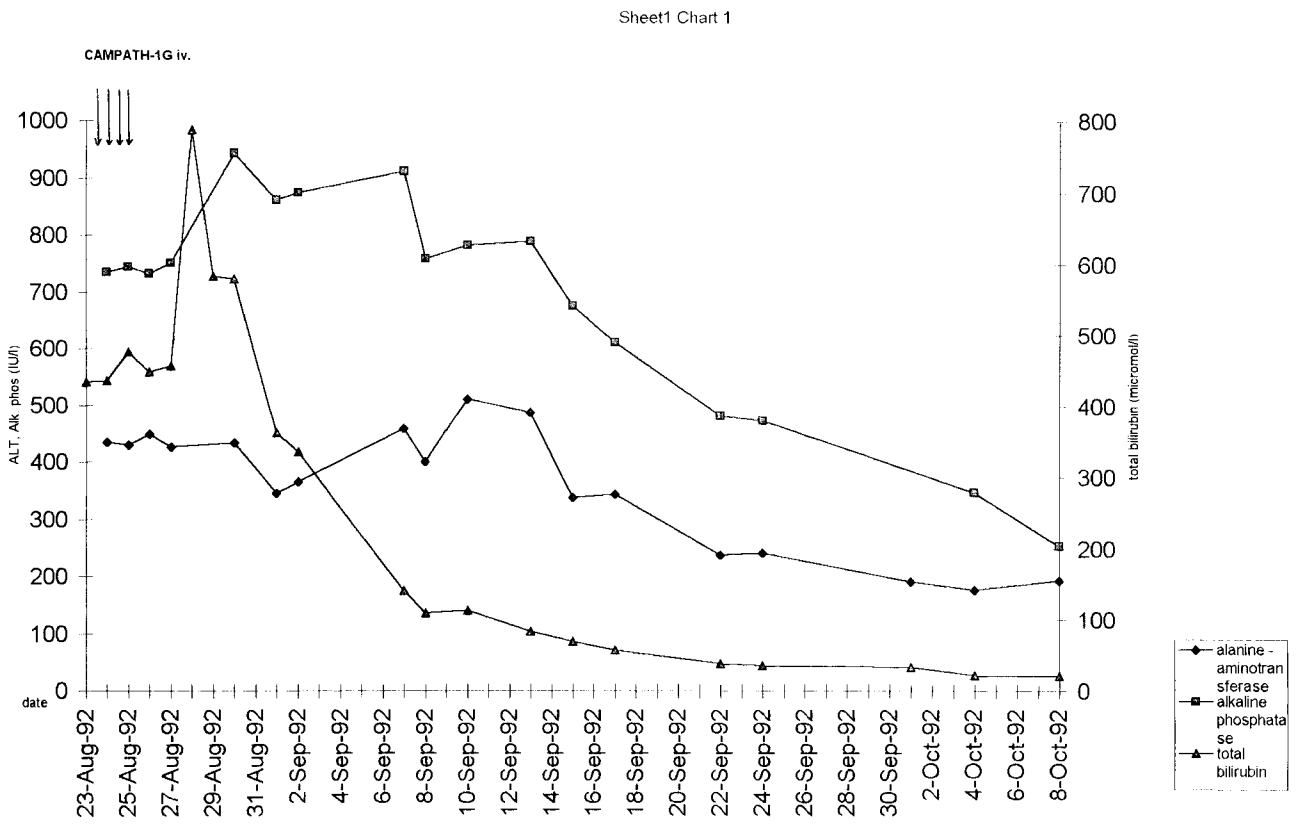

Fig. 1. Response to CAMPATH-1. Drastic improvement of liver function tests following CAMPATH-1 administration.

improved slowly, as well and this therapy was continued. The patient was discharged 1 month later with grade II GVHD, normal bilirubin, ALT 194 U/L, AST 116 U/L, ALP 204 U/L, and GGTP 891 U/L. Gradual and very slow improvement has continued.

Currently, 4 years after BMT, the patient is in hematologic and cytogenetic remission, (including polymerase chain reaction (PCR) negativity) with mild chronic GVHD, localized in the skin and liver.

During the past few years, CAMPATH-1 has been used successfully for the removal of immunocompetent T cells and natural killer (NK) cells, for the prevention of GVHD; in vivo CAMPATH-1 has also been used as an additional immunosuppressive agent in BMT preconditioning [2], and to treat autoimmune disorders, including rheumathoid arthritis [3]. Because of its anti-T and anti-NK activity, we concluded that CAMPATH-1 would also be a good candidate for the treatment of GVHD. In the case presented, CAMPATH-1 administration resulted in significant improvement of grade IV GVHD, manifesting mainly liver involvement. T cells have been previously shown to be involved in various liver pathogenesis and to be able to mediate severe liver damage. Moreover, we and others have demonstrated the ability of CAMPATH-1 to improve hepatitis and liver damage associated with severe aplastic anemia [5].

In light of this case, we suggest including CAMPATH-1G therapy for severe, life-threatening aGVHD when other therapeutic modalities have failed. The next step is to elucidate the role of CAMPATH-1 in anti-GVHD therapy and comfirming these findings on a large group of patients.

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Congenital Afibrinogenemia: Treatment of Excessive Menstrual Bleeding With Continuous Oral Contraceptive

To the Editor: We read with interest the correspondence of Castman et al. [1] about inhibition of ovulation by oral contraceptive in patients with congenital afibrinogenemia, in order to prevent hemoperitoneum. We report our recent experience with such treatment for excessive menstrual bleeding.